

added LiAlH₄ and the mixture was stirred at room temperature under N₂ for 24 hours. Under ice cooling the reaction mixtures was quenched by addition of saturated aqueous NaHCO₃. The resulting slurry was filtered and washed with THF. The solution was concentrated and the residue was brought into CH₂Cl₂. washed with H₂O. dried (MgSO₄) and concentrated to dryness. The residue was purified over preparative TLC (silica gel) CH₂Cl₂:MeOH:TEA=8:1:0.08.

Synthesis of 4,5-diol ceramide: To a solution of ceramide in a mixture of Me₂CO distilled H₂O and t-BuOH. N-Methyl morpholine N-oxide (NMO. 1.2 equivalent) and OsO₄ (catalytic amount) in THF were added. The reaction mixture was stirred at 45° C. for 6 hours and it was quenched by solid NaHCO₃ and the mixture was stirred for 15 minutes. The suspension was filtered and filtrate was dissolved in THF. The solution was washed with brine. The organic solution was separated, dried and concentrated to dryness. The residue was purified over preparative TLC (THF).

What is claimed is:

✓ 1. A liposome having a bilayer comprising a lipid component which comprises a compound having the formula R¹-Y¹-CHZ¹-CH(NY²Y³)-CH₂-Z², wherein:

R¹ is a straight-chained alkyl, alkenyl or alkynyl group having from 5 to 19 carbon atoms in the aliphatic chain;

Y¹ is —CH=CH—, —C≡C— or —CH(OH)CH(OH) —;

each of Z¹ and Z² is independently OH or a conversion-inhibiting group;

Y² is a phenyl group, an alkyl-substituted phenyl group having from 1 to about 6 carbons in the alkyl chain, or an alkyl chain having from 1 to 6 carbons;

Y³ is H or a group having the formula —C(O)R² or —S(O)₂R²;

R² is a straight-chained alkyl moiety selected from the group consisting of —(CH₂)₃CH₃, —(CH₂)₅CH₃, —(CH₂)₇CH₃ and —(CH₂)₉CH₃, or an alkenyl or alkynyl group having from 1 to 23 carbon atoms in the aliphatic chain;

Z² is a phosphorylcholine attachment-inhibiting group selected from the group consisting of -X¹, —OX¹, —X²X³ and —OX²X³:

X¹ is selected from the group consisting of —C(O)H, —CO₂H, CH₃(C(CH₃)₃)₂, Si(C(CH₃)₃)₃, Si(PO₄)₂C(CH₃)₃, a phenyl group, an alkyl-substituted phenyl group having from 1 to 6 carbons in the alkyl chain, an alkyl chain having from 1 to 6 carbons, an amino group, a fluorine, a chlorine, and a group having the formula C(R³R⁴)OH;

X² is selected from the group consisting of CH₂—, C(CH₃)₂—, Si(PO₄)₂—, Si(CH₃)₂—, SiCH₃PO₄—, C(O)— and S(O)₂—;

X^3 is selected from the group consisting of $—C(O)H$,
 $—CO_2H$, $—CH_3$, $—C(CH_3)_3$, $—Si(CH_3)_3$, $—SiCH_3C(CH_3)_3$,
 $—Si(C(CH_3)_3)_3$, $—Si(PO_4)_2C(CH_3)_3$, a phenyl group, an alkyl-substituted phenyl group having
5 from 1 to 6 carbons in the alkyl chain, an alkyl chain having from 1 to 6 carbons, an amino moiety, a
chlorine, a fluorine, or a group having the formula $C(R^3R^4)OH$, wherein each of R^3 and R^4 is independently
10 an alkyl chain having from 1 to 6 carbons, a phenyl group or an alkyl-substituted phenyl group having from 1 to 6 carbons in the alkyl chain;
15 wherein when Z^2 is an amino group, R^2 is an aliphatic chain having from 1 to 9 or from 19 to 23 carbon atoms in the aliphatic chain.
15 and wherein the compound comprises at least about 5 mole percent of the lipid.
2. The liposome of claim 1, wherein R^1 is $CH_3(CH_2)_{12}—$.
20 Y^1 is $—CH=CH—$ and Y^2 is H .
20 3. The liposome of claim 1, wherein Y^3 is $—C(O)(CH_2)_4CH_3$.
4. The liposome of claim 1, wherein the conversion-inhibiting group is $—OSi(CH_3)_2C(CH_3)_3$.
25 5. The liposome of claim 1, wherein the compound has the formula $CH_3(CH_2)_{12}—CH=CH—CH_2Z^1—CH(NHY^3)—CH_2—Z^2$.
30 6. The liposome of claim 5, wherein Y^3 is $—C(O)(CH_2)_4CH_3$, and wherein Z^2 is $—OC(O)CH_3$, $—OC(O)CH_2CH_2CH_3$, $—OC(O)CH(CH_3)CH_3$, or $—OSi(CH_3)_2C(CH_3)_3$.
35 7. The liposome of claim 1, wherein the compound comprises at least about 10 mole percent of the lipid.
8. The liposome of claim 1 comprising an additional bioactive agent.
35 9. The liposome of claim 1, wherein the lipid further comprises vitamin D_3 .
40 10. The liposome of claim 9, wherein vitamin D_3 comprises about 1 mole percent of the lipid.
40 11. The liposome of claim 1, wherein the lipid further comprises a headgroup modified lipid.
45 12. The liposome of claim 1 which is dehydrated.
13. A pharmaceutical composition comprising the liposome of claim 1.
45 14. A method of administering a bioactive liposome to an animal which comprises administering to the animal the pharmaceutical composition of claim 13.
50 15. The method of claim 14, wherein the animal is afflicted with a cancer and wherein the amount of the composition administered comprises at least about 0.1 mg of the compound per kg of the animal's body weight.

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16. A compound having the formula $R^1-Y^1-CHZ^1-CH(NY^2Y^3)-CH_2-Z^2$, wherein:

R^1 is a straight-chained alkyl, alkenyl or alkynyl group having from 5 to 19 carbon atoms in the aliphatic chain;

Y^1 is $-CH=CH-$, $-C\equiv C-$ or $-CH(OH)CH(OH)-$;

Z^1 is OH or a phosphorylcholine attachment-inhibiting group selected from the group consisting of $-X^1$, $-OX^1$, $-X^2X^3$ and $-OX^2X^3$;

Y^2 is H, a phenyl group, an alkyl-substituted phenyl group having from 1 to about 6 carbons in the alkyl chain, or an alkyl chain having from 1 to 10 carbons;

Y^3 is H or a group having the formula $-C(O)R^2$ or $-S(O)_2R^2$;

R^2 is a straight-chained alkyl moiety selected from the group consisting of $-(CH_2)_3CH_3$, $-(CH_2)_5CH_3$, $-(CH_2)_7CH_3$ and $-(CH_2)_9CH_3$, an alkenyl group having from 1 to 23 carbon atoms in the aliphatic chain and an alkynyl group having from 1 to 23 carbon atoms in the aliphatic chain;

Z^2 is OH or a phosphorylcholine attachment-inhibiting group selected from the group consisting of $-X^1$, $-OX^1$, $-X^2X^3$ and $-OX^2X^3$;

X^1 is selected from the group consisting of $-C(O)H$, $-CO_2H$, $CH_3(C(CH_3)_3)_2$, $Si(C(CH_3)_3)_3$, $Si(PO_4)_2C(CH_3)_3$, a phenyl group, an alkyl-substituted phenyl group having from 1 to 6 carbons in the alkyl chain, an alkyl chain having from 1 to 6 carbons, an amino group, a fluorine, a chlorine, and a group having the formula $C(R^3R^4)OH$;

X^2 is selected from the group consisting of CH_2 -, $C(CH_3)_2$ -, $Si(PO_4)_2$ -, $Si(CH_3)_2$ -, $SiCH_3PO_4$ -, $C(O)$ - and $S(O)_2$ -;

X^3 is selected from the group consisting of $-C(O)H$, $-CO_2H$, $-CH_3$, $-C(CH_3)_3$, $-Si(CH_3)_3$, $-SiCH_3(C(CH_3)_3)_2$, $-Si(C(CH_3)_3)_3$, $-Si(PO_4)_2C(CH_3)_3$, a phenyl group, an alkyl-substituted phenyl group having from 1 to 6 carbons in the alkyl chain, an alkyl chain having from 1 to 6 carbons, an amino moiety, a chlorine, a fluorine, or a group having the formula $C(R^3R^4)OH$, wherein each of R^3 and R^4 is independently an alkyl chain having from 1 to 6 carbons, a phenyl group or an alkyl-substituted phenyl group having from 1 to 6 carbons in the alkyl chain;

wherein when Z² is an amino group, R² is an aliphatic chain having from 1 to 9 or from 19 to 23 carbon atoms in the aliphatic chain.

17. The compound of claim 16, wherein R² is an alkyl chain.

18. The compound of claim 16, wherein R¹ is CH₃(CH₂)₁₂-.

19. The compound of claim 16, wherein Y¹ is -CH=CH-.

20. The compound of claim 16, wherein Y² is H.

21. The compound of claim 16, wherein Y³ is -C(O)R².

22. The compound of claim 16, wherein Z¹ is OH.

23. The compound of claim 22, wherein Z² is a group having the formula -X²X³ or -O-X²X³.

24. The compound of claim 23, wherein Z² is -OC(O)CH₃, -OC(O)CH₂CH₂CH₃, -OC(O)CH(CH₃)CH₃, or -OSi(CH₃)₂C(CH₃)₃.

25. The compound of claim 24, wherein Z² is -OSi(CH₃)₂C(CH₃)₃.

26. The compound of claim 22, wherein Z² is a group having the formula -X¹ or -OX¹.

27. The compound of claim 16 having the formula CH₃(CH₂)₁₂-CH=CH-CH₂Z¹-CH(NHY³)-CH₂-Z²

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28. The compound of claim 27, wherein Z^1 is OH and Y^3 is a group having the formula $-C(O)R^2$.

29. The compound of claim 28, wherein Y^3 is $-C(O)(CH_2)_4CH_3$.

30. The compound of claim 27, wherein Z^2 is $-OSi(CH_3)_2C(CH_3)_3$, $-OSi(PO_4)_2C(CH_3)_3$, $-C(O)CH_3$ or $-OC(O)CH_2CH_2CH_3$.

31. A pharmaceutical composition comprising the compound of claim 16.

32. A liposome having a bilayer comprising a lipid component, said lipid component comprising at least about 5 mole percent of the compound of claim 16.

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